



CASE REPORTS

Carcinoma of the Colon Complicating Ulcerative Colitis with Five-Year Survival

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THE GREAT PESSIMISM that surgeons generally have with regard to patients who have carcinoma complicating ulcerative colitis prompted this study. The present case exemplifies many of the features reported when these conditions co-exist, but it is exceptional in that the patient had two extensive carcinomas yet was still living more than five years after operation.

Report of a Case

A 42-year-old, mentally retarded white man entered Riviera Hospital May 25, 1959. He had had almost constant diarrhea, with ten to 12 bowel movements a day since age 14, and in that time he had had essentially no treatment or medical observation.

No abnormalities were noted on palpation of the abdomen. Sigmoidoscopic examination showed diffuse friability and inflammation of the mucosa and a polypoid lesion at the 22 cm level. Biopsy of a specimen from the lesion was reported as adenocarcinoma.

The hemoglobin content on admission was 9.3 gm per 100 ml of blood. X-ray examination with

barium enema showed an absence of haustrations and shortening of the whole colon. There was a large filling defect in the right transverse colon and also a defect in the sigmoid colon. The terminal ileum was dilated, the walls were very smooth and there was an absence of mucosal markings.

At operation the masses in the hepatic flexure and in the sigmoid colon were observed, and there was no evidence of gross spread of carcinoma outside the field of surgical excision. A total abdominal colectomy (including about two and a half feet of terminal ileum) and an end-to-end ileo prostostomy four inches above the anus were carried out.

Pathological examination of the resected specimen showed the ileal mucosa to be irregular, focally flattened and somewhat granular for the distal 11 cm. There was a polyp of the cecum (microscopically identified as a pseudopolyp with inflammation of the stalk). In the right colon there was an 8 x 12 cm villous mass which, histologically, was observed to be a fairly well differentiated adenocarcinoma extending into the muscularis. Finally, 12 cm from the distal end of the resected colon there was a 5 cm mass which microscopically was seen to be a well differentiated mucus-secreting adenocarcinoma extending into the muscularis. There was no lymph node metastasis.

In the more than five years since the operation the patient has passed two or three semi-formed stools each day and he has not had any anemia or loss of weight. Sigmoidoscopic examination, including biopsy of the rectum and anastomotic area, has been done a number of times and no evidence of residual or recurrent carcinoma has been observed.

Discussion

The reported incidence of recurrence of carcinoma of the colon in patients who have ulcerative colitis is extremely variable, depending upon whether the group studied was treated conservatively (in which case the incidence is determined mainly from autopsy statistics) or treated surgically (in which case the group is likely to be heavily weighted with patients who were deemed likely to

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have carcinoma). Slaney and Brooke¹⁵ studied 358 patients with carcinoma in a total group of 9,469 patients with ulcerative colitis and found an incidence of 3.8 per cent, in contrast to the incidence of 0.06 per cent of carcinoma of the colon in the general population. Stated in another way, Shanks and Bagen¹⁴ said that carcinoma of the colon is about 30 times more common in patients with ulcerative colitis than in the general population.

However, if the patient has had ulcerative colitis for ten years or more, there is a 25 per cent to 50 per cent incidence of carcinoma in surgical series:

<i>Investigator</i>	<i>Year</i>	<i>Per Cent with Carcinoma</i>
Cattell and Colcock ³	1955	45.5
Consell and Dukes ⁴	1952	36.0
Lyons and Garlock ⁵	1951	28.0

The longer the duration of ulcerative colitis, the greater the incidence of carcinoma. For example, Shands and Bagen¹⁴ found an average duration of 15.3 years in 73 cases and only 11 per cent of the patients had had carcinoma less than five years and 24 per cent less than ten years. Furthermore, there appears to be a distinctly higher incidence of carcinoma if the patient had symptoms of ulcerative colitis before the age of 16 years.^{10,12,17} The average age at the time of diagnosis of carcinoma is apt to be as much as 20 to 30 years younger than that found in the general population affected by cancer.^{13,15,17} Slaney¹⁵ reported an average age of 41.1 years in 112 cases of carcinoma in patients with ulcerative colitis as contrasted with an average age of 63.2 years in 710 cases of carcinoma of the colon in the general population. Most investigators¹³⁻¹⁷ report an almost equal incidence of carcinoma in men and women with ulcerative colitis, in contrast to the usual sex incidence of two males to one female for carcinoma of the colon and rectum in the general population.

Many theories⁶ have been advanced to explain the malignant degeneration in ulcerative colitis. Probably the most tenable, as expressed by Kasich, Weingarten and Brown,¹¹ is that the repeated destruction and regeneration of mucosa eventually gives rise to atypical cells and then carcinoma. Dukes and Lockhart-Mummery⁸ emphasized that the regeneration of epithelium is in excess of normal and there is an abundant "vasoformative" tissue to support growing epithelium. Dukes⁷ noted that fragments of mucosa may become buried in submucosa or muscularis, and he conjectured that this misplaced mucosa may be a predisposing factor in the development of malignancy. Brooke² pointed out that many other conditions in which epithelium is debased by either infection or scar may eventually give rise to carcinoma—for example, chronic

leg ulcers, ulcers associated with burns and chronic sinus tracts.

Despite the high association of pseudopolyps and carcinoma (36 per cent reported by Bagen and Gage,¹ 78 per cent by Goldgraber and coworkers⁹), most observers believe that pseudopolyps in themselves have no greater pre-malignant potential than the remainder of the abnormal colonic mucosa.

Pathology

Slaney and Brooke¹⁵ reported that it may be difficult to recognize small areas of carcinoma with the naked eye in the resected specimen. Carcinomas associated with ulcerative colitis may show wide submucosal spread. About half of the cases show multicentricity of carcinoma,^{14,15} as contrasted with an incidence of 4.7 per cent¹³ of multicentricity of carcinoma of the colon developing in the general population. The multiple carcinomas may have a differing histologic appearance, and there is a greater incidence of mucoid (colloid) carcinoma (12 per cent).¹⁶ There is about an even distribution of carcinomas throughout the whole colon, without the usual higher incidence in the rectum and sigmoid, but there appears to be a peculiar predilection for origin from the appendix.¹⁶ There have also been isolated reports of squamous cell carcinoma² and lymphosarcoma¹ associated with ulcerative colitis. The inflammatory, vascular base of ulcerative colitis on which carcinoma develops, produces not only early submucosal spread and early hematogenous and lymphatic metastases, but also early, direct extension through the wall of the colon and over peritoneal surfaces. Tidrick¹⁷ reported widespread peritoneal metastasis in four of six cases, and Rosenquist and coworkers¹³ reported that in only 11 of 26 patients was resection of any kind possible.

Diagnosis

Carcinoma of the colon developing in a patient with chronic ulcerative colitis is pernicious in that it frequently develops after many years of apparent remission, and the improvement may be radiological as well as clinical.¹³ The improved conservative treatment of ulcerative colitis with antibiotics, steroids and blood may be conducive to these protracted periods of apparent remission—and eventually a higher incidence of carcinoma.

The only symptom strictly referable to the carcinoma is pain resulting from obstruction or perirectal extension, which indicates advanced carcinoma. Furthermore the usual diagnostic aids are often not very helpful. There is not the usual predilection of carcinoma to develop in the rectum or sigmoid, thereby making a larger proportion of cases accessible to sigmoidoscopic examination. The

stenosis and friability caused by ulcerative colitis may further add to the difficulty and hazard of sigmoidoscopy and biopsy. Radiologically, the distortions caused by stenosis and pseudopolyp formation may lead to a false impression of carcinoma; conversely, the carcinoma is apt to be very focal or sessile and superficially spreading, making it very difficult to demonstrate. Rosenquist and co-workers¹³ expressed belief that x-ray evidence of shortening of the colon may give premonitory evidence of developing carcinoma. Goldgraber and coworkers⁹ reported over 40 per cent failure to detect cancer by radiological means.

Treatment

In the majority of these patients carcinoma is so far advanced that even palliative resection is impossible. When feasible, most observers^{2,14} favor proctocolectomy and ileostomy rather than ileo-proctostomy. This preference for including the rectum is based not only on the chances of carcinoma developing in the rectal stump, but also on doubts that the ileo-proctostomy would function satisfactorily over a long period. We elected ileo-proctostomy in the present case because of a feeling that the patient's inability to care for an ileostomy himself would, perhaps, require institutional care.

Prognosis

In 1959 Slaney and Brooke,¹⁵ in a review of the literature, found that of 304 patients with carcinoma associated with ulcerative colitis only 13 survived five years or more, making a five-year survival rate of 4.2 per cent. In his own series, Brooke² reported seven of the twenty-five patients with ulcerative colitis and carcinoma were still living, but in none of these seven cases was the carcinoma diagnosed preoperatively, and in all seven the lesion was "probably early." Similarly White (cited by Brooke²) reported eight early survivors, in none of whom was the diagnosis made preoperatively. Rosenquist¹³ reported that 22 of 26 patients with carcinoma in association with ulcerative colitis were dead within the first year following diagnosis of the cancer. In a unique series by Bagen and Gage¹ 178 patients with ulcerative colitis and carcinoma were seen at the Mayo Clinic between 1913 and 1958. Operations for cure were performed in 101 cases, with 32 patients surviving five years or more.

Conclusion

The chances of carcinoma developing in patients who have had ulcerative colitis for ten to twenty years is about one in three, irrespective of a remission of symptoms. There is great difficulty in diagnosing curable carcinoma associated with ulcerative colitis on the basis of either change in symptoms,

physical examination or barium enema. Generally there is a very poor prognosis reported for five-year survival, especially when the carcinoma attains definite demonstrable proportions.

In view of the above observations, we have to agree with Brooke,² Rosenquist¹³ and others that colectomy is indicated if the patient has had ulcerative colitis for more than ten years (especially if symptoms of ulcerative colitis started before age 20) with the permanent radiographic changes of ulcerative colitis (especially, permanent shortening of the colon). If the surgeon elects abdominal colectomy and ileo-proctostomy instead of proctocolectomy and ileostomy as the treatment in the individual case, permanent follow-up with frequent proctoscopic examination is necessary.

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